

AMENDMENTS TO THE SPECIFICATION

In the specification, at page 6, lines 20-29, please delete the existing, once amended paragraph and replace with the following, twice amended paragraph after implementing the following changes:

In addition to the new immunization and screening techniques provided herein, antibodies that bind to aminophospholipids and anionic phospholipids and have a number of advantageous properties can now be identified by competition and/or functional assays using the monoclonal antibodies 1B9, 1B12, 3B10, 2G7, 7C5, 9D2 or 3G4. Currently, the 1B12, 3B10, 9D2 and 3G4 antibodies are preferred. Certain of these antibodies do not require serum for phospholipid binding. The monoclonal antibodies 9D2 and 3G4 are more preferred, with monoclonal antibody 3G4 (ATCC 4545) currently being the most preferred. To identify additional antibodies that compete with any of the foregoing antibodies, preferably 3G4, the preferred assays are currently competition assays based upon an ELISA, a number of which are described herein, and working examples of which are disclosed.

In the specification, at page 9, lines 8-17, please delete the existing, once amended paragraph and replace with the following, twice amended paragraph after implementing the following changes:

In certain aspects, the antibodies will effectively compete with the monoclonal antibody 1B9, 1B12, 3B10, 2G7, 7C5, 9D2 or 3G4, preferably with 9D2 or 3G4, and most preferably with 3G4 (ATCC 4545), for binding to an aminophospholipid or anionic phospholipid, preferably PS, or will have the aminophospholipid or anionic phospholipid binding profile of the monoclonal antibody 1B9, 1B12, 3B10, 2G7, 7C5, 9D2 or 3G4, preferably of 9D2 or 3G4, and most preferably of 3G4, as set forth in Table 4. Certain antibodies will not be serum dependent, i.e., will not require serum to bind to the aminophospholipid or anionic phospholipid; not be derived from a patient with a disease, and will not significantly inhibit coagulation reactions *in vitro*, cause significant thrombosis *in vivo* or have lupus anticoagulant activities.

In the specification, at page 22, lines 14-17, please delete the existing, once amended paragraph and replace with the following, twice amended paragraph after implementing the following changes:

All Certain selection criteria, as used herein, are preferably conducted in the absence of serum, to avoid the drawbacks with generating antibodies that could mimic the pathological antibodies of patients, which bind to aminophospholipids or anionic phospholipids in conjunction with proteins.

In the specification, at page 64, lines 29-35, please delete the existing, once amended paragraph and replace with the following, twice amended paragraph after implementing the following changes:

Certain of the antibodies of the present invention have been particularly selected on the basis of not binding to aminophospholipids and anionic phospholipids in combination with protein cofactors, but rather are "true" anti-phospholipid antibodies. ~~The~~ Certain of the antibodies of the invention do not bind or displace the protein cofactors from the phospholipids and are therefore safe for administration. Indeed, mice treated with the antibodies of the invention at high doses for prolonged periods showed no changes in coagulation capability, yet mice respond with APS when injected with anticardiolipin or lupus anticoagulant antibodies.

In the specification, at page 65, lines 21-28, please delete the existing, once amended paragraph and replace with the following, twice amended paragraph after implementing the following changes:

In order to generate antibodies to aminophospholipids and anionic phospholipids with advantageous properties and/or reduced or essentially no side effects, the present invention provides preferred immunization and screening methods. Other immunization techniques and antibodies have been reported in the literature (Umeda *et al.*, 1989; Igarashi *et al.*, 1991; Rote *et al.*, 1993), including those with reported specificity for the type of fatty acid chains involved

(Levy *et al.*, 1990; Qamar *et al.*, 1990). However, the present immunization techniques, and particularly the selection of certain antibodies that are not serum dependent, provide particular benefits.

In the specification, from page 180, line 29 to page 181, line 4, please delete the existing, once amended paragraph and replace with the following, twice amended paragraph after implementing the following changes:

The pathogenic anti-phospholipid antibodies that circulate in patients with antiphospholipid syndrome are believed to bind to PS, PE and other phospholipids in combination with proteins, such as β_2 -glycoprotein I, prothrombin, kininogens, prekallikrein and factor XI (Rote, 1996; Sugi and McIntyre, 1995; 1996a; 1996b). β_2 -glycoprotein I and prothrombin bound to PS are reported to be the primary antigens for anti-cardiolipin antibodies and lupus antibodies, respectively. Certain of the antibodies of the present invention have been particularly selected on the basis of not binding to aminophospholipids and anionic phospholipids only in the presence of serum proteins. The Therefore, by binding to the phospholipid component, certain of the antibodies of the invention are contemplated for use in antagonizing or competing with the pathogenic antibodies in such patients, thus displacing the pathogenic antibodies from their phospholipid-protein targets in the body.

In the specification, at page 220, lines 16-22, please delete the existing, once amended paragraph and replace with the following, twice amended paragraph after implementing the following changes:

The 1B9, 2G7 and 7C5 antibodies behave essentially the same. These antibodies recognize only PS and require serum or serum proteins for binding to PS. The binding of 1B9, 2G7 and 7C5 to various phospholipids was assayed only in the presence of 10% bovine serum, whereas binding of the other antibodies was tested either in the absence or in the presence of serum. For the 9D2 antibody, the presence of serum does not change preference in binding to a particular phospholipid. The 9D2 antibody binds to PS in the absence of serum.

In the specification, at page 277, lines 15-20, please insert the following paragraph:

A certain aspect of 9D2 and like antibodies stems from the inventors' realization that desirable antibodies should preferably be selected using a screen to identify antibodies that bind to PS-coated plates as strongly in the presence of serum as in the absence of serum.